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Effect of folic acid on appetite in children: Ordinal logistic and fuzzy logistic regressions

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ABSTRACT

Objective: Reduced appetite and low food intake are often a concern in preschool children, since it can lead to malnutrition, a leading cause of impaired growth and mortality in childhood. It is occasionally considered that folic acid has a positive effect on appetite enhancement and consequently growth in children. The aim of this study was to assess the effect of folic acid on the appetite of preschool children 3 to 6 y old.
Methods: The study sample included 127 children ages 3 to 6 who were randomly selected from 20 preschools in the city of Tehran in 2011. Since appetite was measured by linguistic terms, a fuzzy logistic regression was applied for modeling. The obtained results were compared with a statistical ordinal logistic model.
Results: After controlling for the potential confounders, in a statistical ordinal logistic model, serum folate showed a significantly positive effect on appetite. A small but positive effect of folate was detected by fuzzy logistic regression. Based on fuzzy regression, the risk for poor appetite in preschool children was related to the employment status of their mothers.
Conclusions: In this study, a positive association was detected between the levels of serum folate and improved appetite. For further investigation, a randomized controlled, double-blind clinical trial could be helpful to address causality.

Introduction

Poor appetite in young children is a major concern of parents [1,2]. In developing countries, reduced appetite and low food intake often are reported in children [3,4]. Reduced appetite and inappropriate food intake can lead to malnutrition [5], a major public health problem in the developing world and an underlying factor of mortality in children under the age of 5 [6–9].

Poor appetite might be caused by micronutrient deficiency, including iron or folic acid deficiency [10]. The relationship between poor appetite and folic acid deficiency may be mediated through the effect of folic acid on cell growth, particularly cells of the gastrointestinal (GI) tract. The gastrointestinal tract is where

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the synthesis and secretion of peptide hormones such as PYY occur, which are influential in regulating appetite [11], but the mechanism through which serum folic acid levels affects appetite is not quite clear.

Based on studies that have shown serum folate effects on appetite and growth in children [1,12], some pediatricians in Iran prescribe folic acid empirically as an appetite-enhancing drug for underweight children with poor appetite [1], although this association is not yet well established. This cross-sectional study aimed to determine whether there is a relationship between the level of folic acid and appetite status in children ages 3 to 6.

In practice, appetite status is basically evaluated by verbal reports and linguistic variables. The borderlines of categories of linguistic variables are not crisp [13,14]. New soft methods are needed to handle such vague variables. Fuzzy regression model is a soft method that can be implemented for their modeling.

In the current study, parents were asked to evaluate the state of their childrens' appetite by means of linguistic variables rather than exact ones. In our point of view, the borderline between subcategories of appetite status that has been reported by parents is vague. Because fuzziness must be considered in modeling systems where human estimation is influential [15], it is preferred to implement fuzzy logistic regression for modeling and evaluating the effect of folic acid and other covariates on appetite. In the present study, statistical ordinal logistic (cumulative logit model) and fuzzy logistic regression were employed to investigate the association between serum folate and appetite status in preschool children.

Material and methods

Study population and sampling

The study sample included 127 children ages 3 to 6 y, who were randomly selected from 20 preschools in the city of Tehran, the capital of the Islamic Republic of Iran, during 2011. Eligibility for inclusion was based on being healthy according to medical history and examination by a pediatrician. Participants with acute intestinal infections, acute respiratory failure, chronic renal failure, active liver disease, hemolysis of red blood cells, intestinal parasites, and fever were excluded from the study.

The study protocol was approved by the Medical Ethics Committee of National Nutrition and Food Technology Research Institute. Written informed consent was obtained from the parents of all participating children at the beginning of the study.

Anthropometric measurements

Anthropometric measurements were taken by trained staff using standardized methods. Body weight was measured for each child to the nearest 0.1 kg, wearing underwear, with a calibrated electronic scale (Seca, Hamburg, Germany maximum estimated error [d] = 100 g). Height was measured, with bared feet, with an accuracy of 0.1 cm, using a wall-mounted portable harpenden stadiometer (Holtain Ltd., UK). Body mass index (BMI) was calculated as weight in kg divided by the square of height in meters (kg/m^2). Information on demographic characteristics was obtained through interviewing parents at enrollment in the study. The participant's age was calculated in months based on the date of birth reported by the mother.

Laboratory measurements

A 2-mL non-fasting blood sample was drawn from each child in the morning. Blood samples were collected from the cubital vein. Samples were drawn into tubes containing ethylenediaminetetraacetic acid (ETDA) and were stored at 8°C. The tubes were protected from light. The samples were delivered to the laboratory of the Research Institute for Endocrine Sciences (RIES) of Shahid Beheshti University of Medical Sciences in less than 2 h after sampling. The blood samples were centrifuged at 3000g for 10 min and the plasma was frozen at −80°C. The plasma was analyzed for serum folate by a Gama counter device together with the radioimmunoassay (RIA) technique (DRG kit, United States). The sensitivity of the RIA method was 0.6 ng/mL. The coefficient of variation for serum folate was 5.6%.

Appetite determination

Children's appetite was assessed by asking their mothers the following question: "How do you describe the amount of food that normally has been eaten by your child in the last few days: very little, little, average, much, or very much."

A rating scale (1–21) was used to rate the degree of appetite. Mothers were asked to circle the number that indicated their child's level of appetite during the last few days. Lower scores indicated less hunger and lower appetite.

Data analysis

Modeling the effect of folic acid on the status of the child's appetite was determined through statistical ordinal logistic and fuzzy logistic regressions. Details of fuzzy logistic regression are explained in the next section. Multiple linear regression analysis was used for modeling the effect of serum folate on the perceived level of appetite, which was evaluated by the 21-point rating scale.

Fuzzy logistic regression

In traditional statistics, in order to regress a binary response variable with two categories on a set of explanatory variables $X = (x_1, x_2, ..., x_p)$, a binary logistic regression model can be used. In binary logistic regression, the response variable $y_i = 0, 1$; i = 1,2, …, n; has binomial distribution, and it can take the value of 1 with a probability of success π, or the value of 0 with probability of failure $1 - \pi$. The logit transformation of π is used for modeling the relationship between the predictor and response variables [16,17], and the form of the model is as follows:

$$\ln\left(\frac{\pi}{1-\pi}\right) = b_0 + b_1x_1 + ... + b_px_p \quad (1)$$

in which the expression $\pi/1 - \pi$ is called the probabilistic odds of characteristic 1.

In some practical studies, the response variable is measured by linguistic terms such as very low, low, medium, high, and very high, rather than by precise numbers. These linguistic terms detect the status of each case relative to the binary response categories (i.e., having the mentioned characteristics or not). When participants' status relative to response variable is evaluated by linguistic terms, the binary response cannot be defined precisely. Therefore, Bernoulli distribution cannot be assumed for such responses, so the probability of success (i.e., fully having the mentioned characteristic) cannot be calculated. Therefore, the probabilistic odds are meaningless [14]. Moreover, it is not realistic to use quantitative symbolic numbers for the subjective qualitative terms of a linguistic variable, because this could leave out important information for modeling [18].

A novel approach to this problem, which was initially proposed by Taheri and Mirzaei Yeganeh [19] and Pourahmad et al. [13,14], is to rate the possibility of success for each observation by defining a proper fuzzy number for each term of the linguistic variable. These fuzzy numbers should be defined in such a way that their support covers the whole range of 0, 1. A brief description on fuzzy numbers can be found in the Appendix.

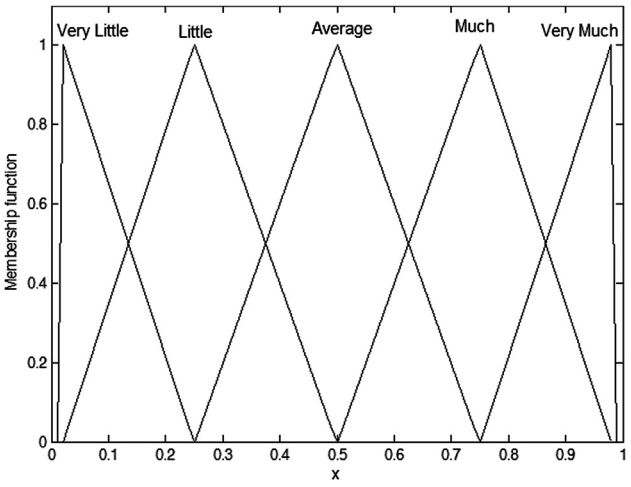

Fig. 1. Membership functions of the linguistic terms for child's appetite.